Incidence of $\dot{V}O_2$max Responders to Personalized versus Standardized Exercise Prescription

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ABSTRACT

WEATHERWAX, R. M., N. K. HARRIS, A. E. KILDING, and L. C. DALLECK. Incidence of $\dot{V}O_2$max Responders to Personalized versus Standardized Exercise Prescription. *Med. Sci. Sports Exerc.*, Vol. 51, No. 4, pp. 681–691, 2019. **Introduction**: Despite knowledge of cardiorespiratory fitness (CRF) training responders and nonresponders, it is not well understood how the exercise intensity prescription affects the incidence of response. The purpose of this study was to determine CRF training responsiveness based on cohort-specific technical error after 12 wk of standardized or individually prescribed exercise and the use of a verification protocol to confirm maximal oxygen uptake ($\dot{V}O_2$max). **Methods**: Sedentary adult participants (9 men, 30 women; 48.2 ± 12.2 yr) completed exercise training on 3 d·wk^{-1} for 12 wk, with exercise intensity prescribed based on standardized methods using heart rate reserve or an individualized approach using ventilatory thresholds. A verification protocol was used at baseline and 12 wk to confirm the identification of a true $\dot{V}O_2$max and subsequent relative percent changes to quantify CRF training responsiveness. A cohort-specific technical error (4.7%) was used as a threshold to identify incidence of response. **Results**: Relative $\dot{V}O_2$max significantly increased ($P < 0.05$) from 24.3 ± 4.6 to 26.0 ± 4.2 and 29.2 ± 7.5 to 32.8 ± 8.6 mL·kg^{-1}·min^{-1} for the standardized and individualized groups, respectively. Absolute $\dot{V}O_2$max significantly increased ($P < 0.05$) from 2.0 ± 0.6 to 2.2 ± 0.6 and 2.4 ± 0.8 to 2.6 ± 0.9 L·min^{-1} for the standardized and individualized groups, respectively. A significant difference in responsiveness was found between the individualized and standardized groups with 100% and 60% of participants categorized as responders, respectively. **Conclusions**: A threshold model for exercise intensity prescription had a greater effect on the incidence of CRF training response compared with a standardized approach using heart rate reserve. The use of thresholds for intensity markers accounts for individual metabolic characteristics and should be considered as a viable and practical method to prescribe exercise intensity. **Key Words:** TRAINING RESPONSIVENESS, EXERCISE NONRESPONDERS, VENTILATORY THRESHOLD, HRR, VERIFICATION PROTOCOL

Low cardiorespiratory fitness (CRF) has been shown to be a predictor of future cardiovascular disease (CVD) incidence and mortality (1), but substantial evidence exists showing that increasing physical activity and exercise can increase CRF (i.e., maximal oxygen consumption, or $\dot{V}O_2$max) and mitigate adverse health effects (2). However, since the 1980s (3), it has been known that considerable individual variability in CRF training responsiveness occurs after a structured aerobic exercise program, and therefore, not all individuals receive the same health outcomes. Indeed, this variability in CRF adaptations has since been shown in a variety of populations including healthy but untrained adults (4–8), postmenopausal women (9), and overweight and obese men and women (10).

Despite knowledge that individual variability in training responsiveness occurs, the causative mechanisms are not fully understood. Through HERITAGE, it was found that age, sex, race, and initial fitness do not significantly affect changes in $\dot{V}O_2$max response to standardized exercise training (11). However, it was found that $\dot{V}O_2$max responsiveness has a significant genetic component and yielded a maximal heritability estimate of 47% (12). More recently, 21 single-nucleotide polymorphisms were found to explain 49% of the variability in $\dot{V}O_2$max trainability (13). Because genetics do not account for all of the variability in training responsiveness, it has been proposed that the methodology of exercise prescription could play a critical role in eliciting

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a desired or undesirable change in $\dot{V}O_2$max. In the late 1970s, it was shown that using a relative percent method (i.e., percentage of heart rate (HR) reserve, or HRR) for prescribing exercise intensity fails to consider individual metabolic differences (14), yet it is still a recommended approach (15). Recent investigations have proposed a more individualized exercise prescription using ventilatory thresholds to personalize a training regime based on individual metabolic responses (5,6) and therefore enhance the potential benefits of regular physical activity.

Our understanding of individual variability after standardized CRF training is confounded owing to methodological weaknesses of criteria used to determine $\dot{V}O_2$max (16–18). The highest $\dot{V}O_2$peak during a graded exercise test (GXT) has been commonly used to prescribe exercise intensity and evaluate training responsiveness. However, a $\dot{V}O_2$peak value does not always indicate a "maximal" value for aerobic fitness. When only peak values are reported, it is unclear whether postintervention values improve, maintain, or decline. For example, if a participant has a $\dot{V}O_2$peak of 25.0 and 30 $mL \cdot kg^{-1} \cdot min^{-1}$ at baseline and postintervention, respectively, it is not easily understood what true changes occurred in CRF. If the baseline $\dot{V}O_2$ was indeed a peak value and the postintervention $\dot{V}O_2$ was a true maximal value, determination of training effect on aerobic function is not possible because there is no way to retrospectively determine the true baseline maximal value. Therefore, a verification protocol (i.e., a supramaximal test after a GXT) has been proposed to confirm when a "true" maximal effort has been achieved (19–22). Recently, two investigations have incorporated the use of a verification protocol to identify individual differences in training responsiveness after sprint (23) and high-intensity (24) interval training. To our knowledge, however, the use of a verification protocol has not been used when evaluating individual training responsiveness after individualized and standardized steady-state exercise intensity prescription.

Another fundamental issue of understanding individual variability after CRF training is a lack in accepted criteria for what is considered to be a response to quantify "responders" and "nonresponders" or those who have a desirable change compared with an undesirable change in a specific parameter, respectively. Commonly, training responsiveness has been quantified based on absolute changes from baseline to postintervention, but this method does not take into consideration normal day-to-day fluctuations in biological variability and the measurement error of the equipment being used (4,25,26). It has been proposed that to have an all-inclusive definition for incidence of response, the technical error (TE; biological variability and measurement error) must be taken into consideration (25). However, oftentimes when TE error has been used to quantify training responsiveness, the TE has been sourced from previous literature rather than developing one that is specific to the site and cohort being analyzed (4–6). Indeed, this methodology may not be sensitive enough to truly identify CRF training responders and nonresponders. Furthermore, many training investigations only report the group mean ± SD, which fails to address the physical adaptations seen in individual participants. Therefore, it is possible that there could be a misrepresentation of exercise prescription effectiveness on the overall training response when only group differences are reported. Collectively, these issues underpin the need for further study to better understand how an individualized approach to the exercise prescription can augment training responsiveness. Indeed, much needed novel data are required to advance the field of exercise programming. Accordingly, the purpose of the current investigation was to determine CRF training responsiveness (changes in $\dot{V}O_2$max with the use of a verification protocol to confirm true $\dot{V}O_2$max) based on a site- and cohort-specific TE after 12 wk of standardized or individually prescribed exercise. Because of taking into consideration the individual metabolic characteristics, it is believed that the individualized group will have a greater overall responsiveness compared with the standardized group.

METHODS

Men and women were recruited from a community wellness program and from the surrounding community via advertisement at the local university, newspaper, and word-of-mouth to be randomized to one of two experimental groups. Inclusion criteria for participation in the study included being considered low to moderate risk based on the American College of Sports Medicine Standards (15), participation in less than 30 min of moderate intensity physical activity on 3 $d \cdot wk^{-1}$ or less, and between the ages of 30 and 75 yr. Exclusionary criteria included evidence of signs or symptoms suggestive of pulmonary, cardiovascular, or metabolic conditions determined from a standard medical history questionnaire and intake interview. Similar to previous research (27,28), a third group (i.e., the control group) was recruited as a convenience sample separate from experimental participants because of the moral and ethical considerations of withholding a known physiological and psychological benefit (i.e., an exercise intervention) that were interested in the various health indices from the laboratory testing, but not interested in increasing regular exercise or physical activity. Control participants had to meet the same inclusion/exclusion criteria previously mentioned and undergo all of the same laboratory testing at baseline and 12 wk. After the baseline testing, control participants were encouraged to maintain their current physical activity behavior and dietary intake habits.

All participants provided written informed consent before initiation of the study. A detailed description of the study methodology and rationale has been previously published (29). The Auckland University of Technology Ethics Committee (16/264) and the Western State Colorado University Institutional Review Board (HRC2016-01-90R6) approved this study.

Experimental testing. All primary outcome variables were obtained at baseline and week 12. To the best of our

ability, baseline and postprogram testing occurred on the same day of the week and time of day to ensure consistency and mitigate any possible changes due to timing of the testing. Before testing sessions, participants were instructed to refrain from any strenuous exertion and to not consume food or drink, other than water, for 12 h. All postprogram testing took place within 1–4 d of the last exercise training session.

Dietary analysis. During the 12-wk study, participants verbally agreed to not change their regular nutritional intake habits and completed a 3-d dietary recall (two weekdays and one weekend day) at baseline and postprogram. Participants were instructed to record as much detail about the food and drink ingested throughout the 3 d recorded. The dietary recall was used to establish energy intake, percentages of macronutrients, and grams of macronutrients.

Physical activity analysis. At baseline and postintervention, participants completed the International Physical Activity Questionnaire (IPAQ) to establish average physical activity levels (metabolic equivalent (MET) per minute per week) and time spent sitting per day. At baseline, the results of the IPAQ survey and a subsequent discussion about weekly physical activity levels were used in combination to establish whether sedentary behavior inclusionary criteria were met.

Anthropometric measurements and resting HR. Participants were weighed to the nearest 0.1 kg on a medical grade scale, and height was measured to the nearest 0.5 cm using a stadiometer (Tanita Corporation WB-3000, Tokyo, Japan). Resting HR was determined using standardized procedures (15). In summary, participants were seated with back support for 5 min with their feet on the ground and arms supported near heart level. A medical-grade pulse oximeter (Nonin Medical Inc., Plymouth, MN) was used to establish resting HR after the 5 min of rest.

Maximal exercise test and verification protocol. A GXT using a modified-Balke pseudo-ramp protocol on a motorized treadmill (Powerjog GX200, Portland, ME) was completed to determine $\dot{V}O_2$max and threshold measurements. Participants chose a self-selected pace to complete the test. After the completion of a 4-min warm-up with the workload gradually increasing to the starting self-selected speed and an incline of 0%, the incline was then increased by 1% each minute until volitional fatigue was reached. During the GXT, HR was monitored using a chest strap and radiotelemetric device (Polar Electro, Woodbury, NT) and expired air and gas exchange data using a metabolic analyzer (Parvo Medics TrueOne 2.0, Salt Lake City, UT) were continuously recorded and monitored. Before the GXT, the metabolic analyzer was calibrated with a calibration gas mixture (16.00% O_2 and 4.00% CO_2) and room air (20.93% O_2 and 0.03% CO_2) in accordance to the manufacturer's guidelines and instructional manual. After the GXT, the last 15 s of gas exchange data was averaged and considered to be the final data point. Subsequently, the 15-s gas exchange data occurring before the final data point were also averaged. The mean of the two processed data points represented $\dot{V}O_2$max for the GXT. The highest HR reached during the GXT was considered to be the maximal HR, and HRR was calculated by taking the difference between maximal and resting HR.

A verification protocol was used to confirm a true $\dot{V}O_2$max was achieved using methods previously published (19,20). In summary, 20 min after the completion of the GXT, participants were asked to complete a 4-min warm-up followed by a volitional test to fatigue at a constant workload that was 5% higher than the last completed stage of the GXT. The workload was determined by taking the final MET value for the GXT and increasing the speed, incline, or combination of the two to achieve a 5% higher MET value for the verification bout. During the verification protocol, HR and gas exchange data were monitored in the same manner as the GXT. The verification $\dot{V}O_2$max was determined based on the same method as the GXT by averaging the final two 15-s averaged data points. A true $\dot{V}O_2$max was confirmed if the two calculated $\dot{V}O_2$max values from the GXT and verification protocol were within ±3.0%, which is the measurement error of the gas exchange measurements (30). The GXT and verification protocol $\dot{V}O_2$max values were averaged, and this value was used as the participant $\dot{V}O_2$max to identify training responders and nonresponders. If a participant had a difference in $\dot{V}O_2$max values >3.0%, they were asked to repeat the GXT and verification bout protocol within 24–72 h until a difference less than ±3.0% was achieved to confirm true $\dot{V}O_2$max reached.

Determination of ventilatory thresholds. The determination of the first ventilatory threshold (VT1) and the second ventilatory threshold (VT2) were performed based on previously published methods (5,6,29). A visual inspection of the gas exchange data was analyzed to determine VT1 and VT2 using time, ventilatory equivalents of O_2 ($\dot{V}_E/\dot{V}O_2$), and ventilatory equivalents of CO_2 ($\dot{V}_E/\dot{V}CO_2$). VT1 occurred when $\dot{V}_E/\dot{V}O_2$ increased without a concurrent increase in $\dot{V}_E/\dot{V}CO_2$, whereas VT2 was the point that both $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ simultaneously increased. All assessments were completed by two experienced exercise physiologists. If there were conflicting results, the original assessments were reevaluated, and a consensus was agreed upon.

Exercise prescription. Participants were randomized into one of the two experimental groups according to a computer-generated sequence of random numbers stratified by sex. Throughout the 12-wk intervention, participants exercised 3 $d \cdot wk^{-1}$ in an indoor fitness facility on motorized equipment with a set HR and time established based on the GXT results. Participants exercised using a motorized treadmill, elliptical trainer, and/or stationary bike. To equate exercise volume, the exercise duration was based on energy expenditure per kilograms of body weight per week ($kcal \cdot kg^{-1} \cdot wk^{-1}$) to establish an isocaloric volume between groups. The energy expenditure was determined based on matching the prescribed exercise HR to the corresponding energy expenditure from the GXT. For the standardized group, exercise intensity was based on percentages of HRR, whereas the individualized group had an intensity that was established based on

TABLE 1. A summary of the week-to-week exercise prescription for the standardized and individualized groups.

Week	Energy Expenditure, kcal·kg^{-1}·wk^{-1}	Standardized	Individualized
		Target HR, %HRR	Target HR
1	5.6	40–45	HR < VT1
2	8.4	40–45	HR < VT1
3	11.2	40–45	HR < VT1
4	11.2	50–55	HR ≥ VT1 to <VT2
5	11.2	55–60	HR ≥ VT1 to <VT2
6	11.2	55–60	HR ≥ VT1 to <VT2
7	12.6	55–60	HR ≥ VT1 to <VT2
8	14.0	55–60	HR ≥ VT1 to <VT2
9	14.0	60–65	HR ≥ VT2
10	14.0	60–65	HR ≥ VT2
11	15.4	60–65	HR ≥ VT2
12	15.4	60–65	HR ≥ VT2

VT1 and VT2. For the HR intensity when established using VT1 and VT2, the following HR ranges were used:

- Target HR < VT1 = HR range of 10 bpm below VT1 to the HR at VT1
- Target HR ≥ VT1 to < VT2 = HR range of 15 bpm directly between VT1 and VT2
- Target HR ≥ VT2 = HR range of 10 bpm above VT2

A full summary of the week-to-week progression in exercise prescription can be seen in Table 1.

Establishment of the TE for training responsiveness. A site- and cohort-specific TE (combination biological variability and measurement error) was developed from a subgroup from the current investigation. Specific details and results have been previously published (31). In summary, 16 participants completed two baseline testing sessions, as described previously, no sooner than 24 h and no more than 7 d later while maintaining their current lifestyle. The biological variability for $\dot{V}O_2$max was established by determining the coefficient of variability after repeat testing sessions and was found to be 4.7%. Therefore, the TE was established to be 4.7% for $\dot{V}O_2$max and indicating that a participant in our laboratory and within this sample population needs to have a change in $\dot{V}O_2$max greater than 4.7% in order for the training adaptations to be considered meaningful.

Statistical analysis. All statistical analyses were performed using SPSS Version 25.0 (Chicago, IL). Data were reported as mean ± SD. Based on a power calculation previously published (29) and an assumption of a 20% dropout rate, 20 participants were desired for each group. One-way ANOVA testing was used to compare groups at baseline and, where appropriate, Tukey *post hoc* test. The assumption of normality was confirmed by examination of normal plots of the residuals in ANOVA models and Shapiro–Wilk tests (32). Paired-sample *t* tests were used to analyze within-group differences in continuous variables. Between-group difference of the change in continuous variables from baseline to 12 wk was assessed through ANCOVA, with the week 12 values as the dependent variables and the baseline value as a covariate and, where appropriate, a *post hoc* analysis with a comparison of main effects and a Bonferroni adjustment. Subsequent ANCOVA was performed with the percent change in $\dot{V}O_2$max, absolute change in $\dot{V}O_2$max, and relative change in $\dot{V}O_2$max as dependent variables and age, sex, height, weight, body mass index (BMI), and baseline $\dot{V}O_2$max (relative and absolute) as covariates.

Delta values (Δ) are expressed as percent change (posttesting minus baseline value divided by baseline value, multiplied by 100) for relative $\dot{V}O_2$max for experimental groups with participants categorized as follows: 1 as responder (% Δ > 4.7%) or 0 as nonresponder (% Δ ≤ 4.7%). χ^2 Tests were subsequently used to analyze the point prevalence of responders and nonresponders to exercise training separated by exercise intensity group (individualized and standardized) between baseline and 12 wk and a Cramer *V* test to determine effect size.

RESULTS

A total of 49 experimental and 20 control participants were recruited for the investigation. There were 39 experimental participants that completed all of the testing sessions and an adherence of 82.9% ± 5.7% and 86.1% ± 4.7% for the standardized and individualized groups, respectively. Of the 20 control participants recruited, 8 completed all testing sessions. There was considerable attrition with the control group because of participants increasing physical activity and exercise after the baseline testing or obtaining health outcomes from testing and electing to not participate in the follow-up testing session. A summary of the number of participants and rationale for exclusion in the study for each group is highlighted in Table 2.

Baseline and post–12-wk physical and physiological characteristics are presented in Table 3. At baseline, there was a significant difference in $\dot{V}O_2$max (mL·kg^{-1}·min^{-1}) between experimental groups ($F_{2,44}$ = 3.86, P = 0.029) with the mean $\dot{V}O_2$max for the standardized group (24.4 ± 4.6 mL·kg^{-1}·min^{-1}) lower than the individualized group (29.5 ± 7.5 mL·kg^{-1}·min^{-1}). However, neither experimental group differed from the control group at baseline. Dietary intake was comparable (P > 0.05) at baseline across groups. Furthermore, there were no significant within-or between-group changes (P > 0.05) in dietary intake from baseline to 12 wk, as presented in Table 3.

Intensity and exercise duration fidelity for both experimental groups were very high, as shown in Figure 1. Only during week 3 for the standardize group, the actual mean minutes completed was 3 min less than the target range for that week.

Changes in $\dot{V}O_2$max. After the 12-wk intervention, both experimental groups significantly improved CRF. Relative $\dot{V}O_2$max significantly increased from 24.3 ± 4.6 to 26.0 ± 4.2 mL·kg^{-1}·min^{-1} (t_{19} = −3.93, P = 0.001) and 29.2 ± 7.5 to

TABLE 2. Number of participants recruited and rationale for exclusion of data.

	Control	Standardized	Individualized
Participants recruited	20	25	24
Participants who completed the study	8	20	19
Rationale for exclusion of participants:			
Unrelated medical issues	2	1	2
Did not achieve ≥70% adherence	—	1	3
Self-withdrawal	10	3	—

TABLE 3. Physical and physiological characteristics and dietary intake at baseline and 12 wk for standardized, individualized, and control groups.

	Control (n = 8; Women = 6, Men = 2)		Effect Size Within Group	Standardized (n = 20; Women = 16, Men = 4)		Effect Size Within Group	Individualized (n = 19; Women = 14, Men = 5)		Effect Size Within Group
Parameter	**Baseline**	**Week 12**	**Cohen *d***	**Baseline**	**Week 12**	**Cohen *d***	**Baseline**	**Week 12**	**Cohen *d***
Age, yr	45.6 ± 7.9	—	—	51.2 ± 12.5	—	—	44.9 ± 11.4	—	—
Height, cm	171.7 ± 6.4	—	—	168.3 ± 9.5	—	—	172.1 ± 7.1	—	—
Weight, kg	75.3 ± 15.1	75.1 ± 14.6	0.01	83.9 ± 20.7	83.8 ± 20.3	0.00	80.6 ± 16.2	79.9 ± 15.2	0.04
BMI, $kg \cdot m^{-2}$	25.5 ± 4.5	25.5 ± 4.6	0.00	29.4 ± 5.5	29.4 ± 5.3	0.00	27.1 ± 4.2	26.8 ± 3.8	0.07
Calorie intake, kcal	1327 ± 418	1265 ± 317	0.17	1520 ± 563	1518 ± 500	0.00	1539 ± 493	1555 ± 403	0.04
Carbohydrate, g	136.5 ± 55.0	121.1 ± 41.8	0.32	160.4 ± 60.5	158.8 ± 63.9	0.03	168.2 ± 68.6	164.5 ± 57.2	0.06
Lipid, g	56.0 ± 18.1	54.0 ± 11.9	0.13	61.1 ± 31.2	62.8 ± 26.4	0.06	68.6 ± 23.4	67.5 ± 13.6	0.06
Protein, g	71.7 ± 43.6	55.0 ± 7.6	0.53	64.1 ± 16.4	63.8 ± 22.0	0.02	73.6 ± 36.6	64.8 ± 25.2	0.28
Carbohydrate, %	40.6 ± 5.8	37.9 ± 5.6	0.47	41.7 ± 6.9	40.9 ± 7.8	0.11	43.1 ± 8.2	41.9 ± 6.7	0.16
Lipid, %	38.7 ± 7.5	39.2 ± 7.0	0.07	35.9 ± 9.2	37.1 ± 8.4	0.14	40.7 ± 7.9	40.6 ± 8.1	0.01
Protein, %	22.1 ± 13.4	17.9 ± 3.1	0.43	18.2 ± 6.3	17.8 ± 5.1	0.07	19.6 ± 10.6	16.5 ± 3.8	0.40
Physical activity, $MET \cdot min^{-1} \cdot wk^{-1}$	1354 ± 1018	1176 ± 1109	0.17	831 ± 954	3660 ± 1629*,***	2.12	937 ± 587	3855 ± 2261*,***	1.77
Time sitting, $h \cdot d^{-1}$	6.5 ± 1.2	6.9 ± 2.5	0.20	5.6 ± 2.6	4.4 ± 2.3*,***	0.49	6.3 ± 2.4	5.4 ± 2.4*	0.38
Resting HR, bpm	74.1 ± 7.8	69.5 ± 7.5	0.60	70.0 ± 8.8	68.2 ± 8.0	0.21	68.8 ± 9.7	68.1 ± 11.4	0.07
Maximal HR, bpm	173.9 ± 12.4	170.1 ± 11.1*	0.32	165.2 ± 16.1	164.9 ± 15.1	0.02	170.1 ± 18.4	169.2 ± 14.4	0.05
$\dot{V}O_2$max, $mL \cdot kg^{-1} \cdot min^{-1}$	28.4 ± 4.5	27.7 ± 4.6	0.15	24.3 ± 4.6***	26.0 ± 4.2*,***	0.39	29.5 ± 7.5	32.8 ± 8.6*,***	0.41
$\dot{V}O_2$max, $L \cdot min^{-1}$	2.2 ± 0.7	2.1 ± 0.7	0.14	2.0 ± 0.6	2.2 ± 0.6*,***	0.33	2.4 ± 0.8	2.6 ± 0.9*,***	0.23
% Difference in $\dot{V}O_2$max (GXT and verification)	0.6 ± 1.5	0.0 ± 2.1	—	−0.2 ± 1.8	−0.4 ± 1.8	—	0.2 ± 1.7	−0.7 ± 1.7	—
% Δ in $\dot{V}O_2$max	—	−2.3 ± 8.5	—	—	7.7 ± 8.3**	—	—	11.4 ± 3.7**	—

Values are mean ± SD.

*Prechange to postchange within-group significant ($P \leq 0.05$) difference.

**Significantly different ($P \leq 0.05$) from the control group.

***Significantly different at baseline from the individualized group.

32.8 ± 8.6 $mL \cdot kg^{-1} \cdot min^{-1}$ ($t_{18} = -9.86$, $P < 0.0001$) for the standardized and individualized groups, respectively. Similarly, there was a significant increase in absolute $\dot{V}O_2$max from 2.0 ± 0.6 to 2.2 ± 0.6 $L \cdot min^{-1}$ ($t_{19} = -3.83$, $P = 0.001$) and 2.4 ± 0.8 to 2.6 ± 0.9 $L \cdot min^{-1}$ ($t_{18} = -6.45$, $P < 0.0001$) for the standardized and individualized groups, respectively. However, although not statistically significant, a 1.5-fold greater increase in the relative percent change in $\dot{V}O_2$max (11.4% ± 3.7% compared with 7.7% ± 8.3%) was found in the individualized group compared with the standardized group.

There were significant between-group differences at postprogram when adjusting for age, sex, and preintervention values for percent change in $\dot{V}O_2$max ($F_{2,44} = 11.799$, $P < 0.0001$), $\dot{V}O_2$max ($mL \cdot kg^{-1} \cdot min^{-1}$; $F_{2,44} = 13.337$, $P < 0.0001$), and $\dot{V}O_2$max ($L \cdot min^{-1}$; $F_{2,44} = 16.536$, $P < 0.0001$). Subsequent group differences can be seen in Table 3.

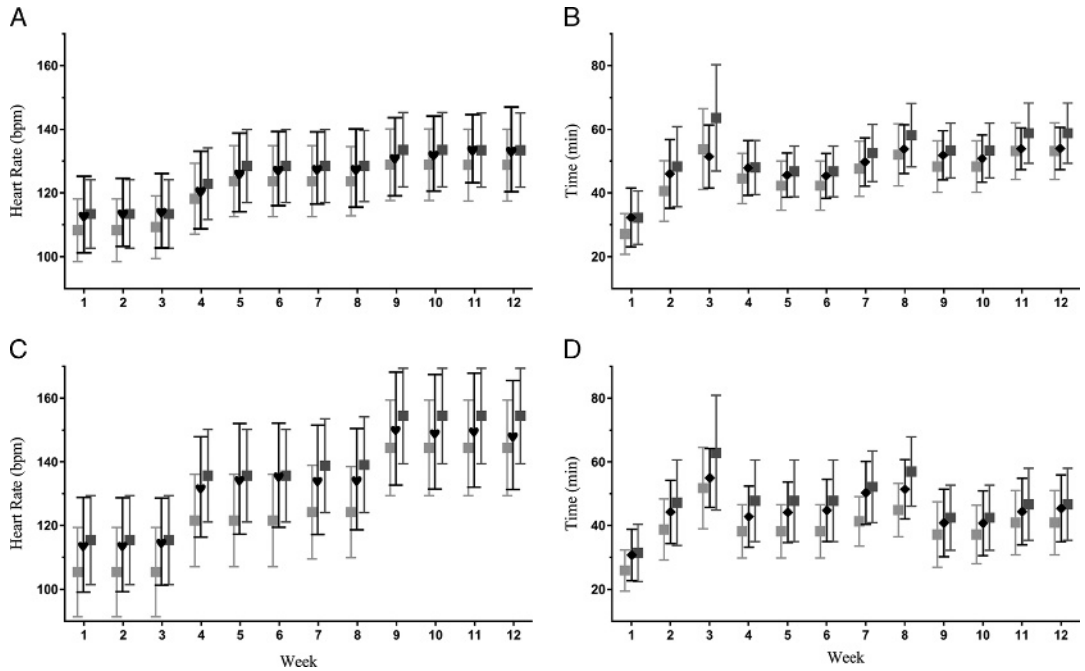

FIGURE 1—The prescribed mean and SD (bars) for the lower and upper limits represented by the light gray and dark gray squares, respectively, for HR and time compared with the mean observed HR (♥) and time (♦) for the standardized (A and B) and individualized (C and D) group.

Prevalence of $\dot{V}O_2$max responders and nonresponders. The prevalences of responders and nonresponders in both standardized and individualized groups are shown in Figure 2. In the standardized group, 60% (12/20) of participants were considered responders with a favorable change in $\dot{V}O_2$max (Δ > 4.7%), and 40% (8/20) were considered nonresponders with a nonmeaningful change in $\dot{V}O_2$max ($\Delta \leq 4.7\%$). All participants (19/19) in the individualized group had a desirable change in $\dot{V}O_2$max ($\Delta > 4.7\%$) and were categorized as responders. Based on the χ^2 analysis, there was a significant difference in incidence of response ($P = 0.002$) and a large effect (Cramer $V = 0.50$) of exercise training strategy on $\dot{V}O_2$max responsiveness. Age, sex, and baseline $\dot{V}O_2$max (absolute and relative) did not have a significant effect on $\dot{V}O_2$max responsiveness.

GXT and verification testing. At baseline and 12 wk, there were only two participants in the individualized group who had a greater than ±3.0% difference between the GXT and the verification test. These participants repeated GXT and verification testing on a separate day to confirm attainment of true $\dot{V}O_2$max. Therefore, the verification procedure confirmed $\dot{V}O_2$max at baseline and postprogram in all participants (47/47). The individual differences in relation to their $\dot{V}O_2$max ($mL \cdot kg^{-1} \cdot min^{-1}$) for the GXT and verification testing at baseline and week 12 are presented in Figure 3.

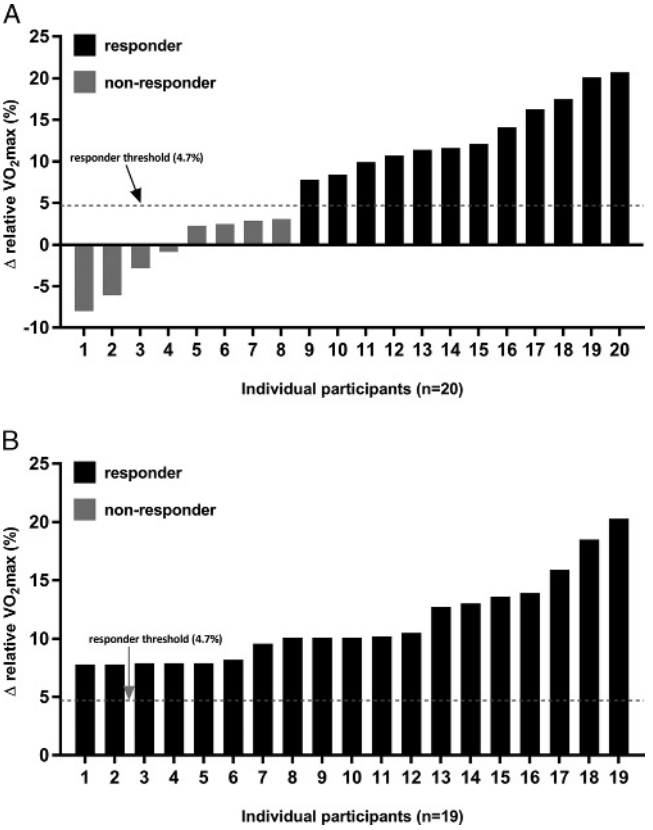

FIGURE 2—Variability in relative $\dot{V}O_2$max responsiveness (% change) to 12 wk of standardized (A) and individualized (B) exercise training. The dashed line indicates the minimum change (Δ > 4.7%) required to be considered a meaningful adaptation in $\dot{V}O_2$max ($mL \cdot kg^{-1} \cdot min^{-1}$).

Changes in other parameters. After the 12 wk, changes in BMI, weight, resting HR, and maximal HR were not significantly different within or between either experimental groups. However, for the standardized group, there was a significant increase in physical activity from 831 ± 954 to 3660 ± 1629 $MET \cdot min \cdot wk^{-1}$ ($t_{19} = -5.95$, $P < 0.0001$), and time spent sitting significantly decreased from 5.6 ± 2.6 to 4.4 ± 2.3 $h \cdot d^{-1}$ ($t_{19} = 2.38$, $P = 0.028$). Similar findings were noted for the individualized group with a significant increase in physical activity from 937 ± 587 to 3855 ± 2261 $MET \cdot min \cdot wk^{-1}$ ($t_{18} = -5.28$, $P < 0.0001$) and decreased time sitting of 6.3 ± 2.4 to 5.4 ± 2.4 $h \cdot d^{-1}$ ($t_{18} = 2.40$, $P = 0.027$). The increase in physical activity reported on the IPAQ at postprogram was expected to increase from baseline because of the prescribed exercise intervention accounting for nearly 1830 ± 463 and 2647 ± 892 $MET \cdot min \cdot wk^{-1}$ for the standardized and individualized groups, respectively. For the control group, there was only a significant difference in maximal HR of 173.9 ± 12.4 to 170.1 ± 11.1 bpm ($t_7 = 3.12$, $P = 0.017$). At postprogram, there were significant between-group differences in physical activity levels ($F_{2,44} = 5.583$, $P = 0.007$) and time spent sitting ($F_{2,44} = 4.304$, $P = 0.20$).

DISCUSSION

To our knowledge, this is the first study to report on the CRF training responses after a standardized and individualized exercise prescription with a cohort-specific threshold for $\dot{V}O_2$max responsiveness and the inclusion of a verification protocol to identify a true $\dot{V}O_2$max. Our innovative data demonstrate that a significant effect of exercise intensity prescription method on the incidence of $\dot{V}O_2$max responders occurred with the individualized group eliciting 100% responsiveness, whereas the standardized group had a 60% incidence of response. These novel findings underscore the importance of a personalized exercise intensity prescription to enhance training efficacy. At the group level, there was a statistically significant positive change in CRF and no difference between groups. However, at the individual level, all participants in the individualized group improved $\dot{V}O_2$max greater than the established TE of 4.7% and were considered $\dot{V}O_2$max responders, whereas 8 of 20 participants in the standardized group failed to elicit a percent change in $\dot{V}O_2$max greater than 4.7% and were considered to be $\dot{V}O_2$max nonresponders. These findings highlight the need to consider individual responses when trying to address best practices to identify exercise prescription methods that promote positive training adaptations rather than only reporting group mean and SD. Furthermore, although not statistically significant, there was a 48% greater improvement in the percent change in $\dot{V}O_2$max at postprogram for the individualized group compared with the standardized group. These changes in CRF are indicative of true maximal changes from baseline to postprogram owing to the incorporation of a verification protocol to confirm a true $\dot{V}O_2$max was achieved. These findings provide further insight to the growing body of

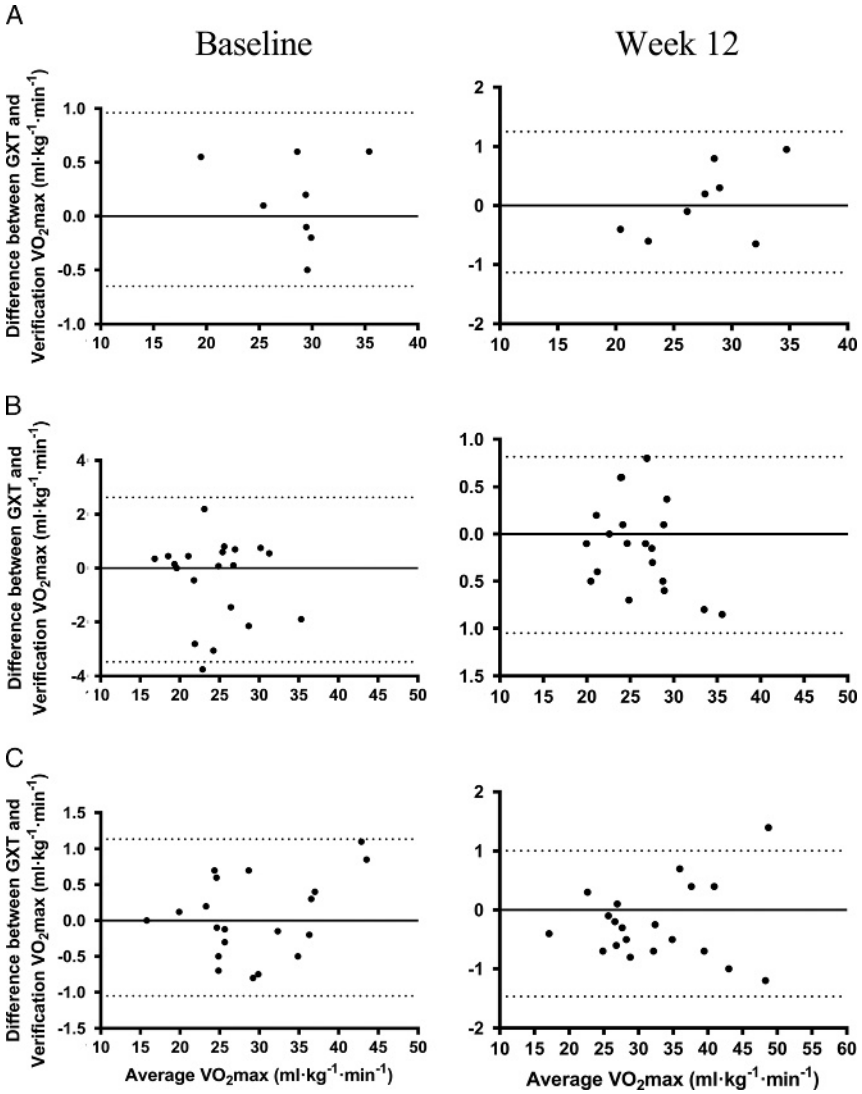

FIGURE 3—Narrowest 95% limit agreement between the GXT and verification protocols at baseline and week 12 for the control (A), standardized (B), and individualized (C) groups. All GXT and verification tests were within ±3.0% (mL·kg^{-1}·min^{-1}).

literature on the importance of personalized or individualized exercise prescription to enhance training efficacy.

Variability in training responsiveness has been linked to the specific exercise prescription and may underpin the individual variability in $\dot{V}O_2$max responsiveness after an exercise training intervention (26). For example, in sedentary postmenopausal women, there was an incidence of nonresponse of 44.7%, 23.8%, and 19.3% when exercising at 50% $\dot{V}O_2$max for 6 months at 4, 8, or 12 kcal·kg^{-1}·wk^{-1}, respectively (9). These results indicate that with an increase in exercise volume, there will be a subsequent improvement in CRF training responsiveness. However, it should be noted that 17 of 88 participants were reported as nonresponders in the highest training volume group, indicating that an even higher training volume may be needed to further increase training responsiveness. Furthermore, Ross and colleagues (33) recently found that CRF nonresponse was eliminated after 24 wk of exercise when the intensity was higher (i.e., 75% of $\dot{V}O_2$peak) compared with a lower intensity (i.e., 50% $\dot{V}O_2$peak) where the incidence of nonresponse was 17.6% when exercising at a fixed amount of 300 and 600 kcal per session for women and men, respectively, in abdominally obese adults. Moreover, they reported that exercise at the recommended amount per week (i.e., 150 min·wk^{-1}) for 24 wk at an intensity of 50% $\dot{V}O_2$peak is not sufficient for CRF training adaptions and yielded nonresponse rates of 38.5% and 17.6% when participants exercised close to 30 and 60 min, respectively. However, at 16 wk, there was a 10.3% nonresponse rate (3/29 participants) in the 75% $\dot{V}O_2$peak group that showed 100% response at 24 wk. More recently, Montero and Lundby (34), found that an extra 6 wk of moderate exercise with an increase in training frequency of 2 d·wk^{-1} can mitigate training nonresponse. However, it should be noted that the TE for maximal wattage was used as a threshold to establish CRF training responsiveness. Indeed, at the end of the first 6 wk of training, all participants training for

60 min on 4 d·wk^{-1} were considered CRF training responders based on increases in maximal wattage. However, if this group was evaluated based on $\dot{V}O_2$max changes, there would have been 3 of 17 participants classified as nonresponders when using the commonly reported 5% TE for $\dot{V}O_2$max (35). Furthermore, at the completion of the second 6-wk training period in which 2 more days a week of training were added, all participants become responders and exceeded the TE for wattage max. However, had these participants been evaluated on the change in $\dot{V}O_2$max, it seems that some of them would not have been considered responders. Although the research evidence suggests that both exercise volume and intensity have a direct effect on CRF training responsiveness, the findings of the present study further highlight that the specific prescription approach is also an influential factor in determining individual responsiveness.

Our findings provide further support on the efficacy of a threshold-based model for exercise prescription. The use of relative percent methods to establish exercise intensity (i.e., %HRmax, %HRR, and %$\dot{V}O_2$max) have shown large interindividual variability in $\dot{V}O_2$max responsiveness (9,33,36–38) and may be due to failing to take into consideration individual metabolic characteristics (14,26,39). For example, when undergoing 60 min of cycling at work rates of 60% and 75% of $\dot{V}O_2$max in healthy male participants, there was a considerable variability in lactate responses with reported coefficient of variations of 52.4% and 41.3%, respectively (39). Similarly, it has been shown that when intensity is calculated as a percentage of the individual anaerobic threshold, ranges of 86% to 118% and 87% to 116% have been identified when exercising at 75% of $\dot{V}O_2$max and 85% of HRmax, respectively (40). Therefore, heterogeneity in training responsiveness will ultimately result from differences in the overall homeostatic stress during the exercise intervention. Katch and colleagues (14) suggested the use of thresholds as markers of exercise intensity to create consistency in the metabolic stimulus in a heterogeneous population. Furthermore, our findings that $\dot{V}O_2$max training responsiveness was superior in the individualized group were consistent with previous findings. Wolpern and colleagues (5) first demonstrated that an individualized approach to exercise prescription using ventilatory threshold markers to establish training intensity elicited greater training responsiveness compared with the HRR method when exercising for 30 min·d^{-1} on 5 d·wk^{-1} for 12 wk. These findings were again shown in a more recent publication using the similar exercise prescription performed 60–75 min·d^{-1} on 3 d·wk^{-1} for 13 wk, but also incorporating resistance and functional training (6). Interestingly, although the exercise training volumes were established with differing criteria (i.e., energy expenditure or time) for these previous and the current investigation, the individualized groups had a 100% response rate to the intervention. However, although all participants in the individualized groups in previous (5,6) and within the current investigation were considered to be responders, there is still variability in overall responsiveness (Fig. 2). This variability may be due to other factors not accounted for in this investigation (i.e., genetics, sedentary behavior outside the exercise training, frequency of interrupting sedentary behavior, etc.). Future research should explore the relationship between these factors and the variability in CRF responsiveness in known responders.

A higher absolute intensity may be a natural byproduct of the threshold-based approach to establishing exercise intensity for an individualized exercise prescription. Indeed, as shown in Figure 1, there is a noticeable difference in the absolute exercise intensities between groups. This discrepancy in absolute exercise HR intensities in the standardized (Fig. 1A) and individualized (Fig. 1C) groups can be directly attributable to the intensity prescription methodology and is an important issue to highlight. It has been suggested that when exercise intensity is anchored to individual ventilatory thresholds, it might better normalize the metabolic stimulus for individuals with varying fitness levels (5,14). However, these same principles are not applied when using the HRR method. Therefore, by using the HRR method, which is currently among the gold standard methods for prescribing exercise intensity, the overall target exercise intensity may be underestimated for the majority of individuals and overestimated for some others. Nevertheless, it is also plausible that between-group differences in exercise HR intensities may have affected the incidence of responders within each treatment group in the present study.

In the present study, participants in the individualized group increased CRF by 1.0 ± 0.5 MET, whereas participants from the standardized group experienced only a 0.5 ± 0.5-MET improvement. These findings are comparable to results from other exercise training studies involving previously sedentary adults. For instance, Bateman et al. (41) reported an improvement in METs of 0.94 and 1.05 in untrained, overweight men and women with mild-to-moderate dyslipidemia, after 8 months of aerobic or a combination of aerobic and resistance training, respectively. More recently, in an investigation using similar exercise intensity prescription methodology to the present study, improvements of 0.49 (HRR group) and 1.11 METs (threshold-based group) were observed after 13 wk of aerobic training for 5 d·wk^{-1} at 30 min·d^{-1} (5). Individual maximal CRF and the associated MET value constitute a potent predictor of CVD prognosis (2). For example, it has been reported that a 1-MET increase in CRF corresponds to 13% and 15% decrements in all-cause mortality and CVD, respectively (42). Accordingly, the differences in CRF improvement in METs in the present study between the individualized and standardized groups represent an important clinical finding, as an optimal method of exercise intensity prescription may contribute to a greater potential to mitigate future CVD events.

Methodologically, two novel factors considered in the current investigation were the use of a site- and cohort-specific TE and a verification protocol to confirm that a true $\dot{V}O_2$max was achieved for all testing sessions. The TE is a conservative approach that takes into consideration the normal day-to-day biological fluctuations and the measurement or assessor error

of the testing procedures. When a change in a physiological parameter exceeds the TE in a positive direction, it can be stated that a true and desired change has occurred. However, if there are factors underpinning methodological issues with the testing to establish the TE (i.e., poor criteria to determine $\dot{V}O_2$max), the TE will not be an accurate assessment of a true change. For example, Ross and colleagues (33) used a cohort-specific TE calculated in consistency with the current investigation with a responsiveness threshold of 0.204 $L \cdot min^{-1}$. However, this TE was calculated based on $\dot{V}O_2$peak rather than $\dot{V}O_2$max and may not accurately dictate when a true change in CRF occurs. The use of $\dot{V}O_2$peak has been criticized in the literature with a change in CRF possibly owing to a greater increase in effort from the expectations of improving after an exercise intervention rather than a true increase in CRF fitness (i.e., $\dot{V}O_2$max) (43). Moreover, primary and secondary criteria used to determine achievement of $\dot{V}O_2$max have also been criticized (16,17). For example, a plateau in $\dot{V}O_2$ at the final stages of a GXT has been considered indicative of $\dot{V}O_2$max; however, there is inconsistency in the literature regarding criteria for a plateau, and a supramaximal verification protocol has been suggested to confirm attainment of a true $\dot{V}O_2$max (18). To our knowledge, we are the first to incorporate a verification bout to confirm that $\dot{V}O_2$max was achieved in the development of our site- and cohort-specific TE. Therefore, it is noteworthy that the change in $\dot{V}O_2$max in the individualized group exceeded the TE in 100% of the participants and elicited true adaptations due to the CRF training intervention.

A review on interindividual differences after an exercise intervention have addressed many methodological and statistical considerations and urged caution with how many investigations have reported the topic (44). Of considerable interest, they highlight that within-subject random variation is inevitable and, in some instances, can account for all of the individual variability in training responsiveness. We have previously demonstrated that different training responsiveness criteria elicit varying percentages of responders and nonresponders to changes in $\dot{V}O_2$max (31), and this topic has been recently evaluated in more depth (45). These findings challenge the notion that observed response variability is the result of random variation in the measured parameters. Therefore, the criteria to establish responsiveness must be specific to the cohort being studied and take into consideration biological fluctuations and measurement error of used testing procedures. Atkinson and Batterham (44) also highlight the importance having a comparator arm (i.e., a control group) to quantify true interindividual differences in training response. Although these methods are appropriate statistical approaches, there are moral and ethical considerations to be addressed with the use of a control group in an exercise intervention in which there is a removal of a known positive physiological factor to improve health. For example, Hecksteden and colleagues (45) evaluated the effects of endurance training with repeated testing on individual responsiveness over a 1-yr period, but used a control group for only 6 months with reported "ethical constraints" as the rationale for not having a control for the intervention duration. We believe that using the methods outlined in the current investigation or performing two to three measurements in all participants at baseline to establish a site- and cohort-specific TE could minimize or, in some instances, eliminate the use of a control group. Furthermore, we suggest continued work with the use of a TE as the threshold for responsiveness but start to focus on individual levels (i.e., individual TE to establish responsiveness). Training responsiveness is an individual and not a group phenomenon, yet all criteria for responsiveness and training interventions have focused on group factors. Further research is warranted to create consistency and acceptance in the scientific community of methodology to accurately examine training responsiveness at the individual level.

Limitations. Because of the randomization process, there is the possibility of selection bias with the principle investigator being aware of which treatment group participants were allocated. However, the use of a verification protocol to confirm a true $\dot{V}O_2$max likely minimized potential selection bias. Another limitation is that training responsiveness was based only on $\dot{V}O_2$max. Training responsiveness is a multifaceted area of study, and future research should focus on a more comprehensive approach to understanding individual variability with consideration of multiple health parameters. The use of a cohort-developed TE, in this instance, can only be used with the assumption that baseline and postprogram TE are indeed the same. Future research should explore whether or not TE changes throughout an exercise intervention. A final limitation was the small sample size for the control group due to difficulties of recruitment and retention of these participants.

CONCLUSIONS

Overall, in previously sedentary adults, 12 wk of aerobic exercise training based on an individualized exercise prescription using ventilatory threshold measures had a greater effect on the incidence of training response compared with a standardized approach using HRR. Although the exact mechanisms are still not entirely understood, it is believed that exercise intensity prescribed with the use of ventilatory thresholds takes into consideration individual metabolic characteristics, which are overlooked when using relative percent methods (i.e., %$\dot{V}O_2$max, %$\dot{V}O_2$R, HRR, etc.). The use of a threshold-based model for steady-state aerobic exercise intensity prescription should be considered in both research and practical applications.

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authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflict of interest. The results of the present study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation and do not constitute and endorsement by the American College of Sports Medicine.

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